

## Amendment #1 to EHA Research Grant Funding Agreement

This is the first Amendment ("Amendment #1") to the EHA Research Grant Funding Agreement, dated 1st of April 2023 (the "Agreement") between the <u>European Hematology Association</u> ("EHA") and <u>Charles University</u> ("Grantee Host Institute") (collectively, the "Parties").

**WHEREAS**, the Parties have entered into the Agreement to fund the project as described in the Agreement,

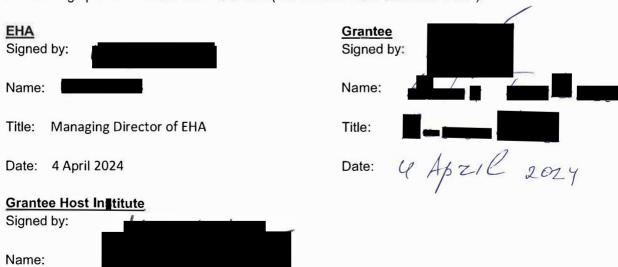
WHEREAS, EHA agreed to make a grant to the Grantee Host Institute to fund the project,

WHEREAS, the Parties wish to amend such Agreement;

**NOW, THEREFORE**, in consideration of the mutual undertakings and agreements hereinafter set forth, the Parties agree to amend the Agreement as follows:

- 1. Parties agree to extend the terms of the Agreement for a further twelve (12) months starting from 1/4/2024 and ending 31/3/2025:
  - a. The grantee will undertake further research as set out in the proposal (Annex 1).
  - b. An additional final project report will be shared with EHA at the end of the extension.
  - c. A grant of 37 205EUR will be paid to the bank account of the Grantee Host Institution on or about 1/4/2024, as supported by the provided financial overview (Annex 2).
- 2. Parties agree that the terms and conditions as set out under this Amendment replace and supersede any other agreement or agreements, oral or written, that the parties may have with respect to the subject matters covered by this Amendment.

IN WITNESS WHEREOF, the Parties hereto have executed this Amendment #1 to be effective, valid and binding upon the Parties as of 1/4/2024 (the "Amendment Effective Date").



Title:

Date: 0 8 -04- 2024





## UNIVERZITA KARLOVA

First Faculty of Medicine **BIOCEV** 

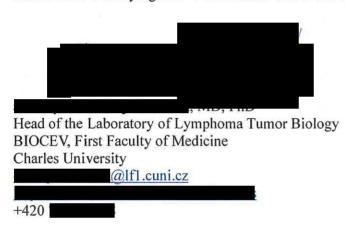
Prumyslova 595, 252 50 Vestec, Czech Republic

	In Vestec 2.2.2024
To: European Hematology Association	
Supplement to EHA Ukraine Bridge Funding renewal application	on -
A brief overview of the extension of the project proposal and aim year.	is to be achieved in the second
During second year, would primarily continue projects. The first project is focused on studies of circulating tumo second one on evaluation of functional effect of lymphoma-associate	or DNA in lymphomas and the
It has been shown that tumor cell-derived cell free DNA (ci could be detected in various non-cellular body compartments and/or disease monitoring and cancer-associated mutations detection. We have panel including 540 genes frequently mutated in various types of lypersonalized Profiling by deep Sequencing, or CAPP-Seq, approaperformance and use for ctDNA detection. In collaboration with five Republic, we are collecting plasma samples for ctDNA evalual stratification and treatment response evaluation. We would further evidence for diagnostic utilization of ctDNA detection in specific clin lymphomas (ctDNA detection in vitreous samples obtained with suspected intraocular lymphomas), CNS lymphomas (cerebrospinal diagnostics and/or therapeutical intervention), or rare cases of T cellulare already being collected and are prepared for ctDNA analysis a	r fluids and could be utilized for ave recently developed our own mphomas (to be used in Cancer ach) and successfully tested its hematology centers in the Czech ation in relation to prognostic er focus to provide additional nical situations as are intraocular in vitrectomy in patients with I fluids collected at the time of I lymphomas. All these samples
classification. We aim a publication related to our first ctDNA-based s	studies to be submitted this year.
Connected to the detection of lymphoma-associated mutati skilled in generation of specific modified lymphoma cell lines to get the functional consequences of these mutations. As a part of convestigating functional consequences of CD79B mutations on once initiation and transmission. In this regard, just recessummarizing the role of CD79A/B molecules in normal as well as movill use his gained skills in cell culture and gene editing methodolog related to CD79A/B mutations. We aim this project (including and a publication to be submitted this year.	netically introduce and evaluate our long-term interest, we are ogenic B-cell receptor signaling ently published a review article alignant B cells.
Additionally, expand developed and established in compand normal human B lymphocytes last year. He engineered feed fibroblasts) to express B lymphocytes survival-promoting and activate to support the expansion of human B lymphocytes. He will finalize e.g., in inhibitors testing (comparing their effect on normal vs. malicell biology questions. We aim to summarize these results in a short of the grant extension period.	der cells (3T3 and L929 murine ing molecules (IL4 and CD40L) evaluation of the system for use, gnant B cells), or for general B



For a collaborative project, also developed an approach for targeted knock out / knock in (KO/KI) at genomic locus of MAGEA1 gene. Two variants of KI were prepared as reporters of MAGEA1 expression: KI of GFP to be expressed instead of MAGEA1 and KI of GFP to be expressed from the MAGEA1 locus at the same time together with MAGEA1 protein. The approach is generally working, and the desired modified cell lines will be produced within next months.

The last but not least aim for the extension of the project is to initialize *in vitro* testing of biological effect of nanoparticles, including rare-earth-based orthovanadate nanoparticles,  $TiO_{2-x}$  nanoparticles with different  $Ti^{3+}(Ti^{2+})/Ti^{4+}$  ratios, and dextran-graft-polyacrylamide/zinc oxide nanosystems to screen their anti-tumor activity against lymphoma cell lines and to uncover molecular mechanisms underlying their eventual anti-cancer effects.







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In Vestec 2.2.2024

To: European Hematology Association	
Supplement to EHA Ukraine Bridge Funding renewal application -	
A financial overview of anticipated costs for the additional year.	
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+420